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| EXAMINER | |
|---|---|
| MURRAY, JEFFREY H | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/561,174 | GEBAUER ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey H. Murray | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 7-16* is/are pending in the application.

4a) Of the above claim(s) *4 and 7-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/19/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. This action is in response to a response to a restriction requirement filed on June 7, 2007. Applicants' election of Group I is acknowledged. The applicant has selected their election expressly *with* traverse. There are sixteen claims pending and four under consideration. Claim 6 has been canceled. Claims 4 and 7-16 are withdrawn from consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. This is the first action on the merits. The application concerns some triazolopyrimidines, a method for their preparation and their use for combating undesirable micro-organisms. The invention also relates to new intermediate products and processes for their preparation.

2. Applicants have made Examiner aware of two errors in the restriction requirement. Applicants have notified the Examiner that the group "VI" appears twice. This is a typographical error. To avoid the renumbering of the entire restriction requirement and possibly adding further confusion, the two Groups will be referred to as VI(a) and VI(b). Applicants were also correct in that the first Group VI, or VI(a) should cite Claim 4 and not Claim 1.

3. Applicant argues that the subject matter of Group I is different than that of the previously mentioned prior art, US 6,576,411 (the '411 patent). This argument is found to not be persuasive. When determining whether a restriction is proper in an international application, it must be decided whether there is "unity of invention." Whether or not any particular technical feature makes a contribution over the prior art and therefore constitutes a "special technical feature," is considered with respect to novelty and inventive step.

Here the Applicants suggest that the core compound is a 6-heterocycle-substituted triazolopyrimidine. In particular, $R^3$ could be anything from a 3-membered epoxide to a 15-membered tricycloheterocycle. As the 6-position could be ANY heterocycle known in the art, it cannot possibly hold any special technical feature. Thus, the Applicants argument is not found persuasive.

4. As mentioned previously the criteria for a proper restriction in an international application is not the same as a U.S. application, thus different rules must be followed. Therefore the criteria mentioned by the Applicants is not proper in the current application. The groups should not be examined for being "independent" or "distinct," rather they should be examined for "unity of invention" and what "special technical feature" may or may not be present. Thus, since the residues attached to the triazolopyrmimidine can be a plethora of different substitutents, there can be no special technical feature attached to any of the residue groups. Since there is no special technical feature, there can be no unity of invention, and thus the applicants arguments are not found persuasive. The restriction is deemed proper and FINAL.

***Priority***

5. Acknowledgment is made of Applicant's claim for foreign priority. This application is U.S. application 10/561,174, filed June 6, 2006, which is a national stage entry of PCT/EP04/06369, filed June 14, 2004, which claims the benefit of foreign priority to DE 10328173.8, filed June 24, 2003.

*Specification*

3. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

**Arrangement of the Specification**

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. The use of the trademarks YIELD GARD, KNOCKOUT, STARLINK, BOLLGARD, NUCOTON, NEWLEAF, ROUNDUP READY, LIBERTY LINK, IMI, STS, and

CLEARFIELD have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

### *Claim Objections*

6. Claim 3 is objected to because of the following informalities:

Claim 3 is lacking the proper punctuation between the alternative members set forth within the claim. Examiner suggests placing commas in between the various R1 groups to properly set them apart. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112, 1st*

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the four compounds synthesized within the specification, does not reasonably provide enablement for all of the compounds and residue groups listed

within the Claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (United States v. Teletronics Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See Ex parte Forman 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

These factors include the following:

1) *Amount of guidance provided by Applicant.* While the Applicant has demonstrated within the application how to make four triazolopyrimidines with a heteroaryl in the 6-position to be used as a possible antimicrobial agent, the generic Claim 1 is massive, and only a small fraction (4) of these compounds are discussed, and their synthesis shown. No reference is made as to how to synthesize any compounds that contain an $R^2$ other than H, an $R^3$ other than a substituted pyrimidine, an X group other than Cl, or a G group other than a sulfide or oxygen.

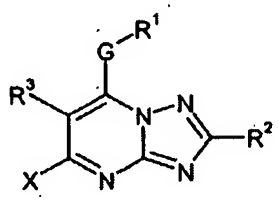
2) *Unpredictability in the art.* It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166. Triazolopyrimidines are currently available drugs for treating depression (antidepressants) such as trazodone; however, tricyclic or similar cyclic anti-depressants have been shown to have side effects such as anticholinergic effects (dry mouth,

blurred near vision, constipation, dysuria), antihistamine effects (weight gain, sedation), antiadrenergic effects (postural hypotension, vertigo, dizziness) and cardiotoxicosis or acute poisoning caused by excessive intake. (Nishibe, et. al. US 6,737,085).

Applicants list that $R_3$ may be an optionlly substituted heterocycle. A reaction is shown within the specification on page 9, as part of the general synthetic scheme to chlorinate the triazolopyrimidine ring. While this may work in the few instant cases, a $POCl_3$ has been known to both formylate and chlorinate heteroaryl ring systems. (Meier, et. al., p. 2 and 5-6). $POCl_3$ may also react to formylate alkenes which are listed in the Claims as potential $R_1$ groups. (Meier, et. al., p. 2-3). The side chains and residues mentioned above have been shown to contain a degree of uncertainty due to the reagents involved in synthesizing the final compounds.

3) *Number of working examples.* Applicant has provided 4 working example compounds of the thousands of triazolopyrimidine compounds that could exist in the applicant's claims. This is a miniscule fraction of the number of compounds that exist in the broad Claim 1.

4) *Scope of the claims.* The scope of the claims involve all of the thousands of compounds of general formula (I):




Thus, the scope of claims is very broad.

5) *Nature of the invention.* The nature of this invention relates generally to triazolo-pyrimidines, a method for their preparation and their use for combating undesirable micro-

organisms. The invention also relates to new intermediate products and processes for their preparation.

6) *Level of skill in the art.* The artisan using Applicants invention would be a physician with a M.D. degree, and having several years of experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making most of the compounds or compositions mentioned in the current application.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(a) as being anticipated by Worthington, et. al., WO 03/039259 which was published on May 15, 2003. The instantly claimed compounds read on Claim 1 of the prior art reference. Claim 1 of the reference publication may have the following: a hydrogen in the 2-position; a halo or alkyl in the 5-

position; a morpholino or pyridyl in the 6-position and a heteroarylthio or heteroaryloxy in the 7-position.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

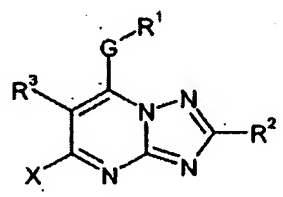
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becher, et. al. (US 5,612,345) in view of Worthington, et. al. (WO 03039259).

The current application recites a variety of triazolopyrimidines for combating undesirable micro-organisms. All of the compounds in the Claims were of the Formula (I):



14. The published reference Becher, et. al. teaches a group of compounds which are similar in scope to the current application. Within Becher, et. al., (Table 1, col.7) similar triazolopyrimidine structures are seen which teach these compounds as being used for a similar purpose (antifungal vs. antimicrobial) as the proposed application.

Becher, et. al. has an identical core structure to the current patent application with two points of diversity. Both the current application and Becher, et. al. can have a triazolopyrimidine core with a hydrogen in the 2-position, a halogen in the 5-position. Where the application and the reference differ is in the 6- and 7-position. The Becher reference suggests a phenyl ring at the 6-position and a halogen in the 7-position. The current application claims a heterocycle at the 6-position and either an oxy or sulfyl derivative at the 7-position.

The second reference, Worthington, et. al. also claims triazolopyrimidines for their use as antifungal agents. Here, the Worthington reference suggests exactly what is missing in the Becher reference. Worthington claims the 6-position may be substituted with a morpholino or piperidino group which would fall under the "heterocyclyl" language of the current application. Likewise, the Worthington reference also claims the 7- position may be substituted with a heteroarythio or a heteroaryloxy group. Both of these groups would satisfy the current application where G can be a S or O and $R^1$ can be a heterocyclyl group.

It would have been obvious to one skilled in the arts at the time of the invention to be motivated to replace the 6-position with a heterocyclyl group like morpholino or piperidino and also to replace the 7-position with a heteroarythio or a heteroaryloxy group. Becher, et. al. combined with Worthington, et. al. show the necessary teachings that suggest replacing the 6- and 7-position groups, and one would have been motivated to substitute in the heterocyclyl

group and heteroarythio or a heteroaryloxy groups respectively, to attempt to enhance activity and afford a positive benefit from the replacement.

***Conclusion***

15. Claims 1-3 and 5 are rejected.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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